CLAIMS

1. A controlled release drug dosage form comprising a core and a coating around said core wherein:

(a) said core comprises a drug-containing composition and a water-swellable composition, each occupying separate regions within said core;

(b) said drug-containing composition comprises a drug, a swelling agent, and a drug-entraining agent;

(c) said coating is water-permeable, water-insoluble, and has at least one delivery port therethrough;

(d) said swelling agent has a swelling ratio of at least 3.5; and

(e) said drug-entraining agent comprises at least 15 wt% of said drug-containing composition.

2. A controlled release drug dosage form comprising a core and a coating around said core wherein:

(a) said core comprises a drug-containing composition and a water-swellable composition, each occupying separate regions within said core;

(b) said drug-containing composition comprises a drug and a drug-entraining agent;

(c) said water-swellable composition comprises a swelling agent and a tableting aid;

(d) said coating is water-permeable, water-insoluble, and has at least one delivery port therethrough;

(e) the mass ratio of said drug-containing composition to said water-swellable composition has a value of at least 1.5;

(f) said water-swellable composition has a swelling ratio of at least 3.5; and

(g) said core has a strength following tableting of at least 3 Kp/cm².

3. A controlled release drug dosage form comprising a core and a coating around said core wherein:

(a) said core comprises a drug-containing composition and a water-swellable composition, each occupying separate regions within said core;

(b) said drug-containing composition comprises a drug and a drug-entraining agent; and

(c) said coating is water-permeable, water-insoluble, has at least one delivery port therethrough, has a water flux (40/75) of at least 1.0×10^{-3} gm/cm²•hr, and a durability of at least 1 Kp/cm².

4. A controlled release dosage form comprising a core and a coating around said core wherein:

(a) said core comprises a drug-containing composition and a water-swellable composition, each occupying separate regions within said core;

(b) said drug-containing composition comprises a drug and a drug-entraining agent; and

(c) said coating is water-permeable, water-insoluble, has at least one delivery port therethrough, is porous and is formed from a substantially homogeneous solution

comprising a solvent, a cellulosic polymer, and a non-solvent.

5. A controlled release drug dosage form comprising a core and a coating around said core wherein:

(a) said core comprises a drug-containing composition and a water-swellable composition, each occupying separate regions within said core;

(b) said drug-containing composition comprises a drug, a drug-entraining agent, and a fluidizing agent, said fluidizing agent having a solubility of at least 30 mg/mL and comprising at least 10 wt% of said drug-containing composition; and

(c) said coating is water-permeable, water-insoluble, and has at least one delivery port therethrough,

wherein at least about 70 wt% of said low-solubility drug is released to a use environment within about 12 hours after introduction to said use environment.

6. A controlled release dosage form comprising a core and a coating around said core wherein:

(a) said core comprises a drug-containing composition and a water-swellable composition, each occupying separate regions within said core;

(b) said drug-containing composition comprises a drug, a solubilizer, and a drug-entraining agent; and

(c) said coating is water-permeable, water-insoluble, and has at least one delivery port therethrough.

7. The dosage form of any one of claims 1-6 wherein said drug-entraining agent is selected from the group consisting of polyols, oligomers of polyethers, mixtures of polyfunctional organic acids, cationic materials, polyethylene oxide, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methyl cellulose, carboxyethylcellulose, gelatin, and xanthan gum.

8. The dosage form of claim 7 wherein said drug-entraining agent is selected from the group consisting of polyethylene oxide, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methyl cellulose, carboxyethylcellulose, gelatin, and xanthan gum.

9. The dosage form of claim 8 wherein said drug-entraining agent is polyethylene oxide.

10. The dosage form of claim 1 wherein said swelling agent is an ionic swelling agent.

11. The dosage form of claim 10 wherein said ionic swelling agent is selected from the group consisting of sodium croscarmellose and sodium starch glycolate.

12. The dosage form of any one of claims 2-6 wherein said drug-containing composition further comprises a swelling agent.

13. The dosage form of claim 12 wherein said swelling agent of said drug-containing composition is an ionic swelling agent.

14. The dosage form of claim 13 wherein said swelling agent of said drug-containing composition is selected from the group consisting of sodium croscarmellose and sodium starch glycolate.

15. The dosage form of claim 14 wherein said swelling agent of said drug-containing composition comprises sodium croscarmellose.

16. The dosage form of claim 14 wherein said swelling agent of said drug-containing composition comprises sodium starch glycolate.

17. The dosage form of any one of claims 1-5 wherein said core includes a solubilizer.

18. The dosage form of claim 17 wherein said drug-containing composition further includes a concentration-enhancing polymer.

19. The dosage form of claim 17 wherein said solubilizer is an organic acid, and said drug has enhanced solubility in the presence of said organic acid.

20. The dosage form of any one of claims 1-5 wherein said drug-containing composition further comprises a solubilizer.

21. The dosage form of claim 20 wherein said solubilizer is an organic acid, and said drug has enhanced solubility in the presence of said organic acid.

22. The dosage form of any one of claims 1-6 wherein said water-swellable composition includes a solubilizer.

23. The dosage form of claim 22 wherein said solubilizer is an organic acid, and said low-solubility drug has enhanced solubility in the presence of said organic acid.

24. The dosage form of claim 23 wherein said drug-containing composition further comprises a concentration-enhancing polymer.

25. The dosage form of any one of claims 1-4 and 6 wherein said drug-containing composition further comprises a fluidizing agent.

26. The dosage form of claim 25 wherein said fluidizing agent is selected from the group consisting of an organic acid, a salt, a sugar, an amino acid, a polyol, and a low-molecular weight oligomer of a water-soluble polymer.

27. The dosage form of claim 26 wherein said fluidizing agent is selected from the group consisting of a sugar and an organic acid.

28. The dosage form of claim 27 wherein said sugar is selected from the group consisting of glucose, sucrose, xylitol, fructose, mannitol, sorbitol, lactose, and maltitol.

29. The dosage form of claim 28 wherein said sugar is xylitol.

30. The dosage form of claim 27 wherein said organic acid is selected from the group consisting of citric acid, lactic acid, ascorbic acid, tartaric acid, malic acid, fumaric acid, and succinic acid.

31. The dosage form of claim 30 wherein said organic acid is citric acid.

32. The dosage form of claim 31 wherein said organic acid is tartaric acid.

33. The dosage form of claim 5 wherein said fluidizing agent is selected from the group consisting of an organic acid, a salt, a sugar, an amino acid, a polyol, and a low-molecular weight oligomer of a water-soluble polymer.

34. The dosage form of claim 33 wherein said fluidizing agent is chosen from the group consisting of a sugar and an organic acid.

35. The dosage form of claim 34 wherein said sugar is selected from the group consisting of glucose, sucrose, xylitol, fructose, mannitol, sorbitol, lactose and maltitol.

36. The dosage form of claim 34 wherein said sugar is xylitol.

37. The dosage form of claim 34 wherein said organic acid is selected from the group consisting of citric acid, lactic acid, ascorbic acid, tartaric acid, malic acid, fumaric acid, and succinic acid.

38. The dosage form of claim 37 wherein said organic acid is citric acid.

39. The dosage form of claim 37 wherein said organic acid is tartaric acid.

40. The dosage form of any one of claims 1, 3, 4, 5 or 6 wherein said water-swellable composition comprises a swelling agent.

41. The dosage form of claim 40 wherein said swelling agent in said water-swellable composition is selected from the group consisting of polyethylene oxide, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methyl cellulose, carboxyethyl cellulose, gelatin, and xanthan gum.

42. The dosage form of claim 40 wherein said swelling agent of said water-swellable composition is an ionic swelling agent.

43. The dosage form of claim 42 wherein said swelling agent of said water-swellable composition is selected from the group consisting of sodium starch glycolate and sodium croscarmellose.

44. The dosage form of claim 2 wherein said swelling agent of said water-swellable composition is an ionic swelling agent.

45. The dosage form of claim 2 wherein said swelling agent of said water-swellable composition is selected from the group consisting of sodium starch glycolate and sodium croscarmellose.

46. The dosage form of any one of claims 1, 3, 4, 5 or 6 wherein said water-swellable composition has a swelling ratio of at least 3.5.

47. The dosage form of claim 46 wherein said swelling ratio of said water-swellable composition is at least 5.

48. The dosage form of claim 46 wherein said swelling ratio of said water-swellable composition is at least 7.

49. The dosage form of claim 2 wherein said swelling ratio of said water-swellable composition is at least 5.

50. The dosage form of claim 2 wherein said swelling ratio of said water-swellable composition is at least 7.

51. The dosage form of claim 2 wherein said tableting aid is selected from the group comprising microcrystalline cellulose, hydroxypropylcellulose, methyl cellulose, and hydroxpropylmethyl cellulose.

52. The dosage form of any of claim 40 wherein said water-swellable composition further includes a tableting aid.

53. The dosage form of claim 52 wherein said tableting aid is selected from the group comprising microcrystalline cellulose, hydroxypropylcellulose, methyl cellulose, and hydroxpropylmethyl cellulose.

54. The dosage form of any of claims 1, 3, 4, 5 or 6 wherein the mass ratio of said drug-containing composition to said water-swellable composition is at least 1.5

55. The dosage form of claim 54 wherein the mass ratio of said drug-containing composition to said water-swellable composition is at least 3.5.

56. The dosage form of claim 2 wherein the mass ratio of said drug-containing composition to said water-swellable composition is at least 3.5.

57. The dosage form of any one of claims 1-6 wherein said low-solubility drug is selected from the group consisting of sildenafil and pharmaceutically acceptable salts of sildenafil.

58. The dosage form of any one of claims 1-6 wherein said low-solubility drug is selected from the group consisting of sertraline and pharmaceutically acceptable salts of sertraline.

59. The dosage form of any one of claims 1-6 wherein said low-solubility drug is the mesylate salt of the drug 4-[3-[4-(2-methylimidazol-1-yl) phenylthio] phenyl]-3,4,5,6-tetrahydro-2H-pyran-4-carboxamide hemifumarate.

60 The dosage form of any one of claims 1-6 wherein said low-solubility drug is 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-3-((3R, 4S)-dihydroxypyrrolidin-1-yl-)-(2R)-hydroxy-3-oxypropyl] amide.

61. The dosage form of any one of claims 1-6 wherein said low-solubility drug is 5-(2-(4-(3-benzisothiazolyl)-piperazinyl)ethyl-6-chlorooxindole.

62. The dosage form of any one of claims 1-6 wherein said low-solubility drug is carprofen.

63. The dosage form of any one of claims 1-6 wherein said drug has a maximum solubility of 20 mg/mL in aqueous solution that has a pH between 1 and 8.

64. The dosage form of any one of claims 1-6 wherein said drug is a low-solubility drug.

65. The dosage form of any one of claims 1-6 wherein said drug is substantially water insoluble.

66. The dosage form of any one of claims 1-6 wherein said drug is sparingly water soluble.

67. The dosage form of any of claims 1, 2, 4, 5 or 6 wherein said coating has a water flux (40/75) of at least 1.0×10^{-3} gm/cm^2-hr.

68. The dosage form of claim 67 wherein said coating has a durability of at least 1 Kp/cm^2.

69. The dosage form of any one of claims 1-6 wherein said coating comprises a hydrophilic cellulosic polymer.

70. The dosage form of claim 69 wherein said cellulosic polymer is selected from cellulose esters, cellulose ethers and cellulose esters/ethers.

71. The dosage form of claim 69 wherein said hydrophilic cellulosic polymer is selected from the group consisting of cellulose acetate, and mixtures of cellulose acetate and a second polymer.

72. The dosage form of claim 71 wherein said hydrophilic cellulosic polymer has a degree of substitution equivalent to 25 to 42 wt% acetyl groups.

73. The dosage form of claim 71 wherein said cellulose acetate has an average molecular weight of at least 45,000.

74. The dosage form of any one of claims 1-6 wherein said coating is formed from a solution having a weight ratio of cellulose acetate to polyethylene glycol of from 9:1 to 6.5:3.5.

75. The dosage form of any one of claims 1-6 wherein said coating is formed from a solution having a water concentration of greater than 4 wt%.

76. The dosage form of claim 74 wherein said solution has a water concentration of greater than 4 wt%.

77. The dosage form of any one of claims 1-6 wherein said coating is formed from a solution having a water concentration of greater than 15 wt%.

78. The dosage form of claim 74 wherein said solution has a water concentration greater than 15 wt%.

79. The dosage form of any one of claims 1-6 wherein said coating includes at least a pore former.

80. The dosage form of claim 79 wherein said pore former is selected from the group consisting of polyethylene glycol, polyvinyl pyrrolidone, polyethylene oxide, hydroxyethyl cellulose, hydroxypropyl methyl cellulose, water-soluble acrylate esters, water-soluble methacrylate esters, and polyacrylic acids.

81. The dosage form of claim 79 wherein said pore former is polyethylene glycol.

82. The dosage form of claim 4 wherein said non-solvent is selected from the group consisting of water, glycerol, C_1 to C_4 alcohols, ethylene glycerol and its oligomers and propylene glycol and its oligomers.

83. The dosage form of claim 4 wherein said solvent is acetone.

84. The dosage form of claim 4 wherein said cellulosic polymer is cellulose acetate.

85. The dosage form of claim 4 wherein said solvent is acetone, said pore former is polyethylene glycol and said non-solvent is water.

86. The dosage form any one of claims 82 and 84 wherein said solution has a water concentration of greater than 4 wt%.

87. The dosage form of claim 86 wherein said solution has a water concentration greater than 15 wt%.

88. The dosage form of any one of claims 1-3, and 5-6 wherein said coating is porous and is formed from a homogeneous solution comprising a solvent, a hydrophilic cellulosic polymer, and a non-solvent.

89. The dosage form of claim 88 wherein said solution further comprises a pore former.

90. The dosage form of claim 89 wherein said pore former is polyethylene glycol.

91. The dosage form of claim 88 wherein said non-solvent is water.

92. The dosage form of claim 88 wherein said solvent is acetone.

93. The dosage form of claim 88 wherein said hydrophilic cellulosic polymer is cellulose acetate.

94. The dosage form of claim 93 wherein said solvent is acetone, said pore former is PEG, and said non-solvent is water.

95. The dosage form of any one of claims 1, 2, 3, 5 or 6 wherein said coating is porous with a dry-state density of less than 0.9 times that of the same coating material in nonporous form.

96. The dosage form of claim 95 wherein said coating has a dry-state density of less than 0.75 times that of the same coating material in nonporous form.

97. The dosage form of claim 95 wherein said coating comprises a polymeric asymmetric membrane comprising a thick, porous region and a dense thin region.

98. The dosage form of claim 4 wherein said coating is porous with a dry-state density of less than 0.9 times that of the same nonporous coating material in nonporous form.

99. The dosage form of claim 98 wherein said coating has a dry-state density of less than 0.75 times that of the same coating material in nonporous form.

100. The dosage form of claim 98 wherein said coating comprises a polymeric asymmetric membrane comprising a thick, porous region and a dense thin region.

101. The dosage form of any one of claims 1-6 wherein said coating has a mass of from 3 to 30 wt% of said core.

102. The dosage form of claim 99 wherein said coating has a mass of from 8 to 25 wt% of said core.

103. The dosage form of any one of claims 1-6 wherein, following introduction of said dosage form to a use environment, no more than 50 wt% of said drug is released to said use environment within 2 hours and at least 60 wt% to said use environment is released within 12 hours.

104. The dosage form of any one of claims 1, 2, 3, 4 or 6 wherein, following introduction of said dosage form to a use environment, at least 60 wt% of said drug is released to said use environment within 12 hours.

105. The dosage form of any one of claims 1, 2, 3, 4 or 6 wherein, following introduction of said dosage form to a use environment, at least about 70 wt% of said drug is released to said use environment within about 12 hours.

106. The dosage form of any one of claims 1-6 wherein, following introduction of said dosage form to a use environment, at least 80 wt% of said drug is released to said use environment within 24 hours.

107. The dosage form of any one of claims 1-6 wherein, following introduction of said dosage form to a use environment, at least 90 wt% of said drug is released to said use environment within 24 hours.

108. The dosage form of any one of claims 1-6 wherein, following introduction of said dosage form to a use environment, at least 95 wt% of said drug is released to said use environment within 24 hours.

109. The dosage form of claim 4 wherein said substantially homogeneous solution further comprises a pore former.

110. The dosage form of claim 4 wherein said non-solvent is present in said substantially homogeneous solution in an amount greater than 20% of its concentration at the cloud point.

111. The dosage form of claim 4 wherein said coating has a dry-state density of less than 90% of the density of a nonporous coating of the same composition.

112. The dosage form of claim 4 wherein said at least one delivery port is formed, at least in part, in the use environment.

113. A controlled release dosage form comprising a core and a coating around said core wherein:

(a) said core comprises a drug-containing composition and a water-swellable composition, each occupying separate regions within said core;

(b) said drug-containing composition comprises a low-solubility drug and a drug-entraining agent; and

(c) said coating is water-permeable, water-insoluble, and has at least one delivery port therethrough; and

(d) wherein said low-solubility drug is in the form of an amorphous dispersion.

114. The dosage form of claim 113 wherein said amorphous dispersion is a solid dispersion of low-solubility drug in a concentration-enhancing polymer.

115. The dosage form of claim 114 wherein said concentration-enhancing polymer is selected from the group consisting of

(a) ionizable cellulosic polymers;

(b) non-ionizable cellulosic polymers; and

(c) vinyl polymers and copolymers having substituents selected from the group consisting of hydroxyl, alkylacyloxy, and cyclicamido.

116. The dosage form of claim 115 wherein said concentration-enhancing polymer is a cellulosic polymer selected from the group consisting of cellulosic esters, cellulosic ethers, and cellulosic esters/ethers.

117. The dosage form of claim 115 wherein said concentration-enhancing polymer is selected from the group consisting of polyvinyl pyrrolidone, polyvinyl alcohol, copolymers of polyvinyl pyrrolidone and polyvinyl acetate and aqueous-soluble cellulosic polymers.

118. The dosage form of any of claims 1 to 6 wherein said low-solubility drug is in the form of an amorphous dispersion.

119. The dosage form of claim 118 wherein said amorphous dispersion is a solid dispersion of low-solubility drug in a concentration-enhancing polymer.

120. The dosage form of claim 119 wherein said concentration-enhancing polymer is selected from the group consisting of

(a) ionizable cellulosic polymers;

(b) non-ionizable cellulosic polymers; and

(c) vinyl polymers and copolymers having substituents selected from the group

consisting of hydroxyl, alkylacyloxy, and cyclicamido.

121. The dosage form of claim 120 wherein said concentration-enhancing polymer is a cellulosic polymer selected from the group consisting of cellulosic esters, cellulosic ethers, and cellulosic esters/ethers.

122. The dosage form of claim 120 wherein said concentration-enhancing polymer is selected from the group consisting of polyvinyl pyrrolidone, polyvinyl alcohol, copolymers of polyvinyl pyrrolidone and polyvinyl acetate and aqueous-soluble cellulosic polymers.

123. A method for treating a disorder, comprising administering to a mammal in need of such treatment, including a human patient, a therapeutically effective amount of drug in a dosage form as defined in claim 1.

124. A method for treating a disorder, comprising administering to a mammal in need of such treatment, including a human patient, a therapeutically effective amount of drug in a dosage form as defined in claim 2.

125. A method for treating a disorder, comprising administering to a mammal in need of such treatment, including a human patient, a therapeutically effective amount of drug in a dosage form as defined in claim 3.

126. A method for treating a disorder, comprising administering to a mammal in need of such treatment, including a human patient, a therapeutically effective amount of drug in a dosage form as defined in claim 4.

127. A method for treating a disorder, comprising administering to a mammal in need of such treatment, including a human patient, a therapeutically effective amount of drug in a dosage form as defined in claim 5.

128. A method for treating a disorder, comprising administering to a mammal in need of such treatment, including a human patient, a therapeutically effective amount of drug in a dosage form as defined in claim 6.

129. A method for treating a disorder, comprising administering to a mammal in need of such treatment, including a human patient, a therapeutically effective amount of drug in a dosage form as defined in claim 113.

130. The dosage form of any one of claims 1-6 wherein said drug-containing composition further includes a concentration-enhancing polymer.

131. The dosage form of claim 130 wherein said concentration-enhancing polymer is selected from the group consisting of

(a) ionizable cellulosic polymers;

(b) non-ionizable cellulosic polymers; and

(c) vinyl polymers and copolymers having substituents selected from the group consisting of hydroxyl, alkylacyloxy, and cyclicamido.